

CLARKE et al  
Appl. No. 09/529,342  
November 24, 2008

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**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-41 (Cancelled).

42. (Currently Amended) A method of detecting a cell type of interest present or potentially present in a sample comprising treating the sample with lipid vesicle particles which are targeted to a targeted cell type to be detected, said particles having at least one layer of enveloping lipids and incorporating a cytolytic peptide, which is non-covalently attached thereto, which peptide, in response to a predetermined extracellular metabolic signal from the targeted cell, if present in the sample, interacts with the layer to act as or mediate the opening of pores or channels within the lipid layer to thereby modulate the permeability of the particles, said particles further incorporating a species which is activated on said modulation of permeability, and monitoring directly or indirectly for the species.

43. (Withdrawn) The method according to claim 42, wherein the cytolytic peptide comprises an integral protein of the lipid layer.

44. (Withdrawn) The method according to claim 42, wherein the cytolytic peptide spans the lipid layer.

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45. (Previously Presented) The method according to claim 42, wherein the cytolytic peptide is non-covalently attached to an outer lipid layer.

46. (Previously Presented) The method according to claim 42, wherein the particles comprise a binding agent capable of binding a particle to the cell type of interest when the particle is targeted thereto.

47. (Previously Presented) The method according to claim 46, wherein the binding agent is an antibody for binding to an antigen on the cell type of interest.

48. (Previously Presented) The method according to claim 42, wherein a portion of said particles have a first binding moiety and a further portion have a second binding moiety which is capable of binding with said first binding moiety whereby said particles are, or are capable of being, aggregated together.

49. (Previously Presented) The method according to claim 48, wherein a collection of particles are aggregated around a cell to be detected.

50. (Previously Presented) The method according to claim 48, wherein the first binding moiety on some particles is avidin or a derivative thereof, and the second binding moiety on other particles is biotin or a derivative thereof.

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51. (Previously Presented) The method according to claim 42, wherein the cytolytic peptide is selected from the group consisting of GALA, Helical erythrocyte lysing peptide (HELP), KALA, and LAGA.

52. (Previously Presented) The method according to claim 42, wherein the cytolytic peptide is N, Myristic-GALA.

53. (Withdrawn) The method according to claim 42, wherein the cytolytic peptide is selected from the group consisting of Amphotericin B, Alamethicin, Gramicidin, Melittin, Nigericin, P25, Polymixin B, Valinomycin, and Vibriolisin.

54. (Previously Presented) The method according to claim 42, wherein the species is a dye.

55. (Previously Presented) The method according to claim 42, wherein the species is an enzyme.

56. (Previously Presented) The method according to claim 55, wherein the enzyme is alkaline phosphatase,  $\beta$ -Galactosidase or asparaginase, or glucose oxidase.

57. (Previously Presented) The method according to claim 42, wherein the species is a co-factor or substrate for an enzyme.

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58. (Previously Presented) The method according to claim 42, wherein the cells to be detected are pathogenic cells.

59. (Previously Presented) The method according to claim 58 for analysing foodstuff for the presence of pathogenic cells.

60. (Previously Presented) The method according to claim 58 for analysing water samples for the presence of pathogenic cells.

61. (Previously Presented) The method according to claim 58 for detecting the presence of pathogenic cells in a human or animal body.

62. (Withdrawn) The method according to claim 42, wherein the metabolic signal comprises a change in ion concentration.

63. (Withdrawn) The method according to claim 62, wherein the ion is  $H^+$ ,  $Na^+$ ,  $Cl^-$ ,  $HCO_3^-$ , or  $K^+$ .

64. (Previously Presented) A method of detecting a cell type of interest present or potentially present in a sample comprising treating the sample with lipid vesicle particles which are targeted to a targeted cell type to be detected, said particles having at least one layer of enveloping lipids and incorporating a cytolytic peptide, which is non-covalently attached thereto,

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which peptide, in response to a predetermined metabolic signal, which metabolic signal comprises a change in pH, from the targeted cell, if present in the sample, interacts with the layer to act as or mediate the opening of pores or channels within the lipid layer to thereby modulate the permeability of the particles, said particles further incorporating a species which is activated on said modulation of permeability, and monitoring directly or indirectly for the species.

65. (Previously Presented) The method according to claim 42, wherein the metabolic signal comprises a change in pH, wherein the pH is above 6.

66. (Previously Presented) The method according to claim 42, wherein the metabolic signal comprises a change in pH, wherein the pH is above 7.

67. (Withdrawn) The method according to claim 42, wherein the metabolic signal comprises a change in gas concentration.

68. (Withdrawn) The method according to claim 42, wherein the metabolic signal comprises a change in carbon dioxide concentration.

69. (New) A method of detecting a cell type of interest present or potentially present in a sample comprising treating the sample with lipid vesicle particles which are targeted to a targeted cell type to be detected, said particles having at least one layer of enveloping lipids and incorporating a cytolytic peptide, which is non-covalently attached thereto, which peptide, in response to a predetermined extracellular metabolic signal from the targeted cell, if present in the

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sample, interacts with the layer to act as or mediate the opening of pores or channels within the lipid layer to thereby modulate the permeability of the particles, said particles further incorporating a species which is activated on said modulation of permeability, and monitoring directly or indirectly for the species,

whercin said cell type of interest is a bacteria.